

# AlphaTAU

(NASDAQ:DRTS)  
**Company Overview**

March 2024

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# The Alpha Tau Mission

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## AlphaDeRT

A novel approach using localized alpha particle radiotherapy designed to precisely destroy solid tumors while sparing surrounding healthy tissue



- ✓ Platform technology may be utilized alone or synergistically with other cancer treatment modalities
- ✓ Radiation delivery can be customized to tumor type and geometry
- ✓ Additional data from multiple clinical trials in various stages in different indications expected in 2024
- ✓ First potential U.S. marketing authorization in 2025, with blockbuster market opportunity across multiple tumor types

# Alpha Tau – Key Investment Highlights

- 1 Proprietary Alpha DaRT designed to safely deliver alpha radiation with localized precision in solid tumors, sparing surrounding healthy tissue
- 2 Broad potential and preclinical evidence supporting evaluation across various solid tumors (skin, pancreas, breast, GBM, etc.) with 23 peer-reviewed pre-clinical papers
- 3 Compelling potential immuno-stimulatory effect and synergetic combination with other therapies
- 4 Over 150 superficial tumors treated to date, with strong results observed. 100% CR seen at 12 weeks in 1<sup>st</sup> US study. Long-term pooled data analysis demonstrates 89% CR rate and 77% 2-year LRFS.
- 5 Favorable safety profile observed, no systemic toxicities, no serious late-onset toxicity.
- 6 Robust clinical-trial strategy with leading global centers, with U.S. pivotal study underway in recurrent cutaneous SCC. Two FDA Breakthrough Device Designations (skin & GBM)
- 7 Solid logistics based on purpose-built manufacturing facilities, built or in planning, in the US, Israel and Asia, with a highly scalable and optimized proprietary production process
- 8 Strong intellectual property (method and device) with over 100 issued and over 200 pending patents worldwide
- 9 Experienced management team, including Alpha DaRT's co-inventors, with expertise in oncology development, manufacturing scale up and commercialization

The logo for AlphaTAU, featuring the word "Alpha" in a dark blue font and "TAU" in a lighter blue font, with a stylized circuit-like graphic element between them.

# Therapeutic Focus

We are focused on delivering solutions to three markets that we believe would be best served by the unique characteristics of the Alpha DaRT

## Localized & Unresectable

- Localized tumors that are not surgical candidates and tumors that recur after surgery and are **resistant to other** therapies, specifically radiotherapy
- Alpha DaRT to be evaluated as a **later line therapy**
- Tumor types include **SCC, H&N SCC and prostate**



## High Unmet Need

- Solid tumors that have **limited treatment options** with limited SOC offering
- Alpha DaRT could potentially target **broad patient populations**
- Tumor types include **GBM and pancreatic cancer**



## Metastatic

- Alpha DaRT would be evaluated for its potential to induce an **immune response** in **metastatic** tumors
- Alpha DaRT would be evaluated **in combination with check point inhibitors** as an adjuvant therapy
- Tumor types include **liver, breast and H&N** (which includes lip, oral cavity, salivary glands, oropharynx & pharynx) cancers



# Development Pipeline

- Our clinical trial strategy involves progressing our lead program (superficial tumors), particularly in the US, and conducting feasibility studies in other tumors to evaluate the Alpha DaRT in tumors of high unmet need or metastatic disease
- FDA Breakthrough Device Designation received for certain uses in skin cancer and GBM

Geography	Indication	Pre-Clinical Research	Feasibility Trial	Pivotal Trial	Marketing Authorization	Anticipated Milestones
North America	Rec. Cutaneous SCC	U.S.				• Complete patient recruitment 2H 2024
	Pancreatic Cancer	Canada				• Interim safety readout in 4Q 2023; targeting trial recruitment completion in 2H 2024
	Liver Metastases	Canada				• First patient targeted in 1H 2024
Israel	Skin & Oral SCC					
	All Skin & Oral Cancers					• Trial completion and submission
	la/mHNSCC (combo with pembrolizumab)					• Feasibility combination trial with Keytruda initiated 4Q 2021; awaiting interim results
	Pancreatic Cancer					• Feasibility trial opened
	Breast Cancer					• Feasibility trial opened
	Lung Cancer					• First patient in feasibility trial targeted 1H 2024
	Brain (GBM + mets)					• Targeting first patient in 2H 2024
Europe	Prostate Cancer					• Opened feasibility trial for focal treatment of recurrent prostate cancer
	Skin Cancers					• Trials underway
	Vulvar SCC					• Trial initiated in Q2 2023
Japan	Pancreatic Cancer					• Trial in planning
	Head & Neck Cancer					• PMDA application sent 4Q 2023, awaiting reply
	Pancreatic Cancer					• Trial in planning (TBD)

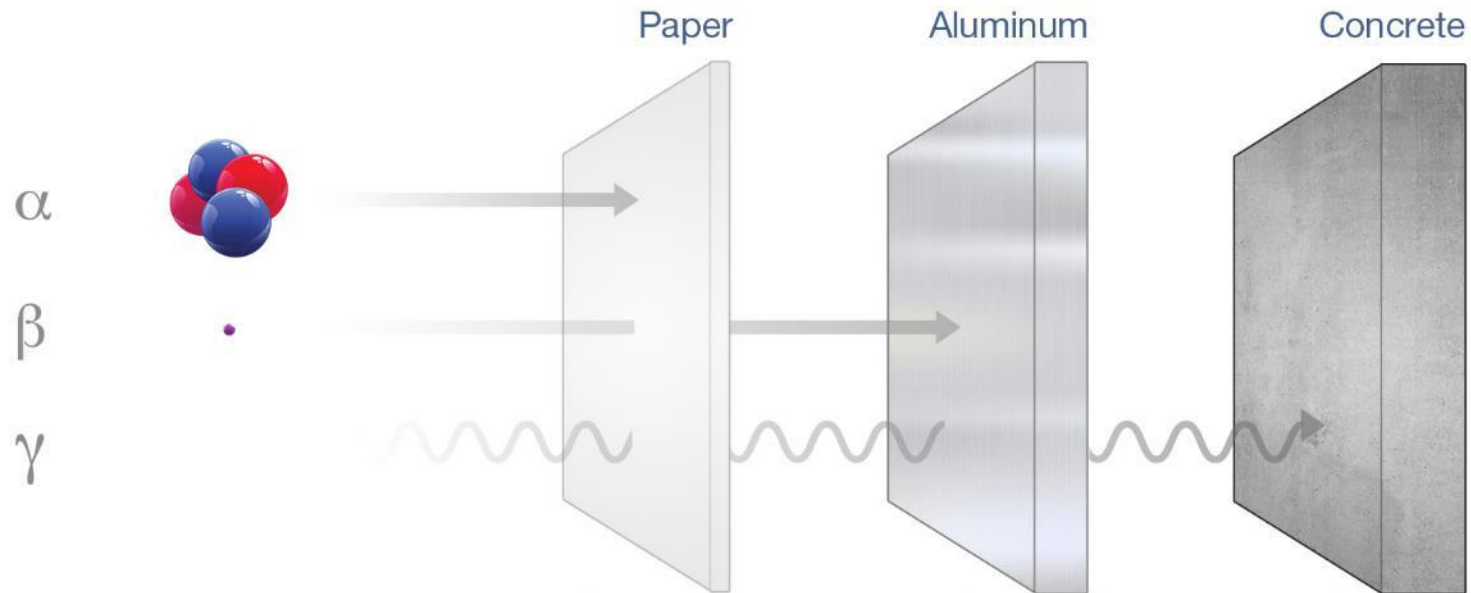
Trials may be conducted across multiple geographies, or there may be interaction between multiple studies (e.g. pooling of long-term response data)

Platform  
Technology

**Alpha DaRT Mechanism of Action and Novel  
Delivery Techniques Make the Treatment  
Broadly Applicable**

# Types of Radioactive Decay

Due to the mass of the alpha particle, in comparison to beta particle, alpha has a low penetration power. This means that the outside layer of the human skin, for example, can block these particles.



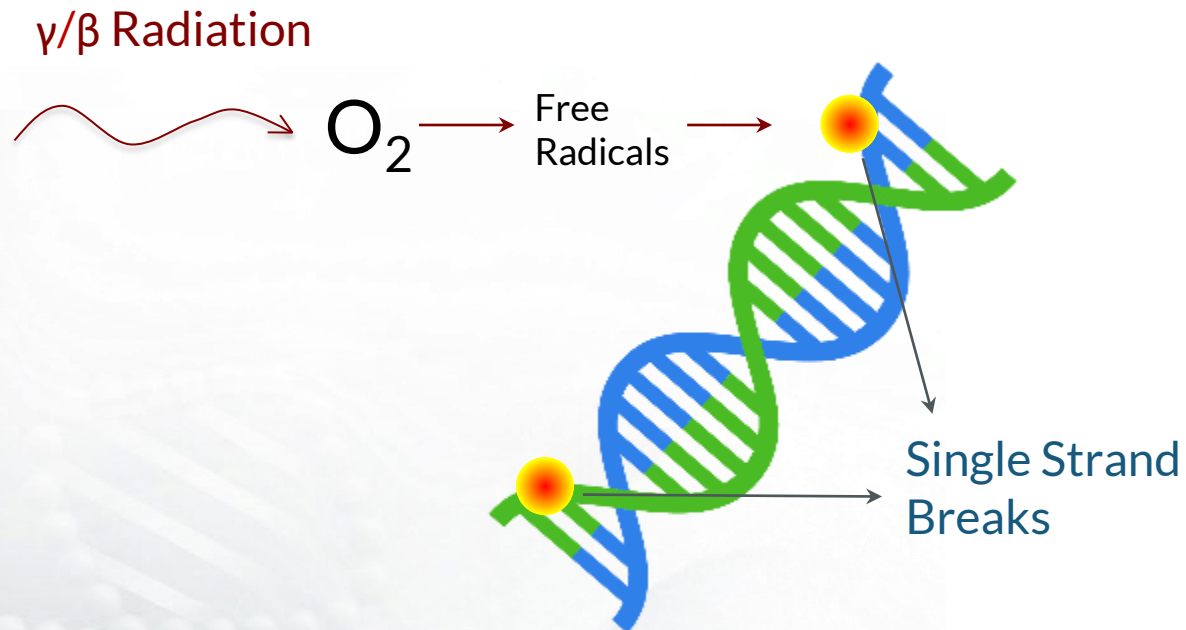


# Potent Alpha Radiation: Extensively Damages the DNA

Local radiation therapy with gamma or beta radiation is a mainstay of cancer treatment, but requires high local dose to be effective, as it primarily relies on single-strand breaks in a process relying on oxygen. Alpha radiation can be significantly more efficient given its ability to destroy both strands of the DNA directly, requiring lower levels of radiation

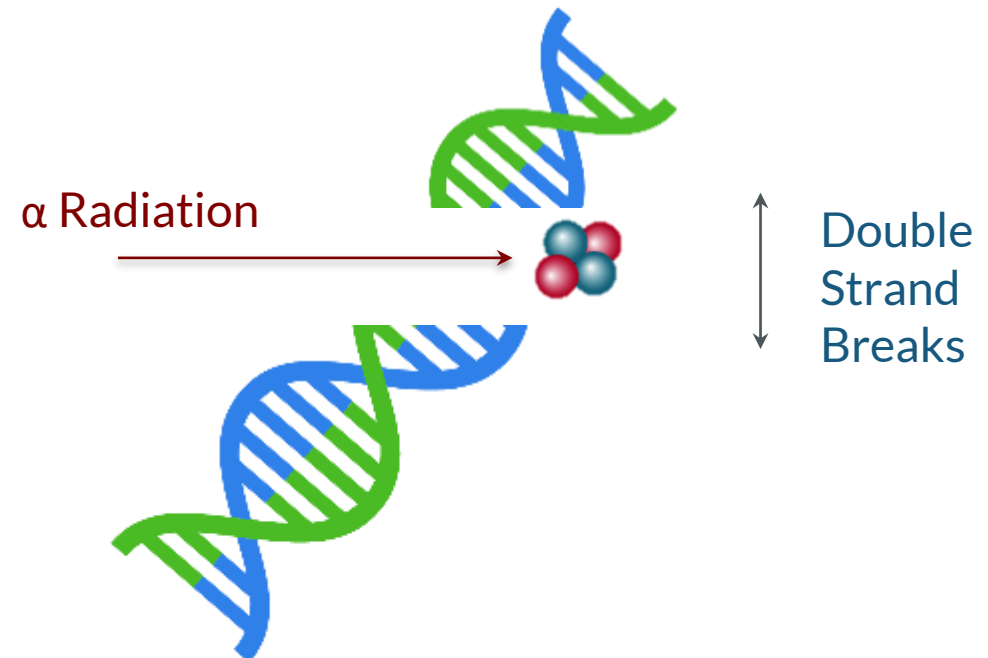
## Conventional Gamma/Beta Radiation

- Indirectly damaging the DNA
- Dependent on oxygen presence
- Repairable single strand breaks



## Alpha Radiation

- Directly damaging the DNA
- Independent of oxygen presence
- Irreparable double strand breaks

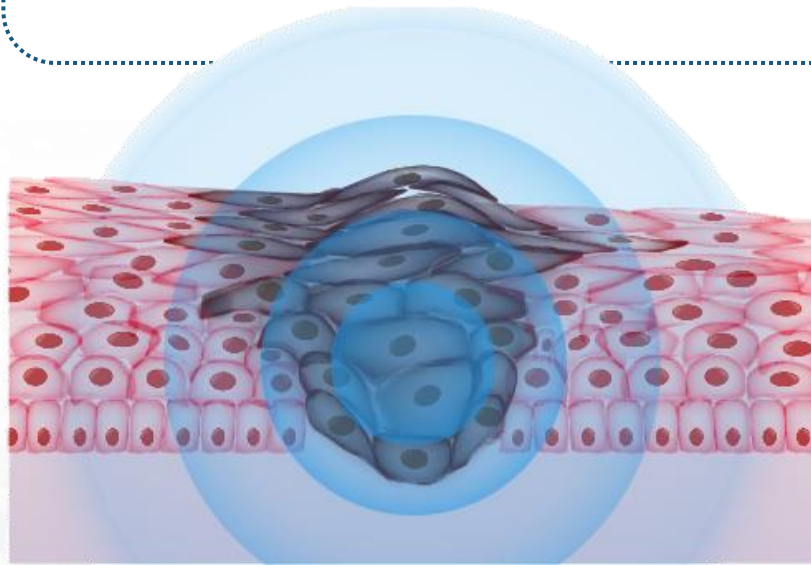


# Alpha Radiation is Focal - Short Range Limits Clinical Use

Whereas beta and gamma radiation can penetrate tissue with sufficient range to facilitate tumor coverage (while risking damage to healthy tissue), alpha radiation has short range in tissue (<100  $\mu\text{m}$ ), which limits its clinical usefulness in local delivery

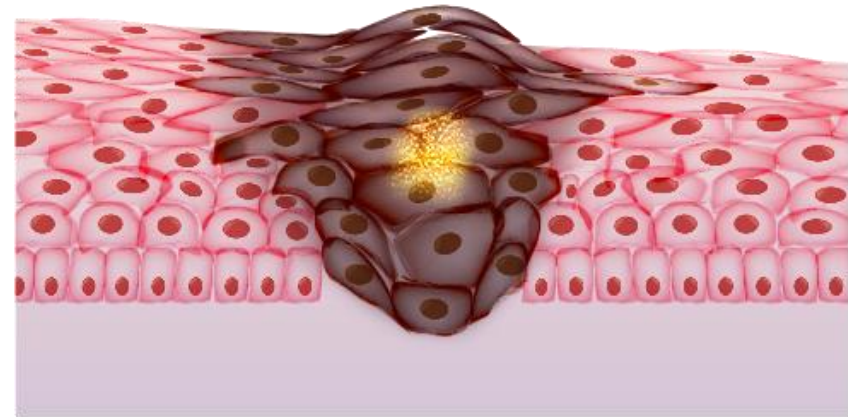
## Beta/Gamma Radiation

Long therapeutic range with risk to surrounding organs



## Alpha Radiation

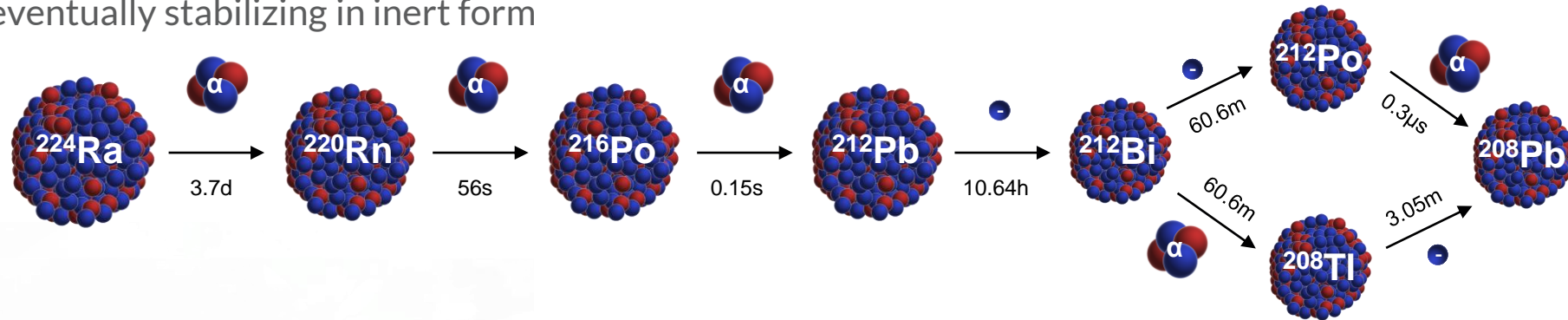
Short range in tissue limits damage to surrounding organs but also limits coverage



# Mechanism of Action of the Alpha DaRT Technology

## $^{224}\text{Ra}$ Decay Chain

- Alpha DaRT leverages the innate decay chain of Radium-224
- The decay chain of Radium-224 includes four alpha particles
- Radium-224 has a half-life of ~3.7 days, while the remaining decay chain has a total half-life of approximately 12 hours, before eventually stabilizing in inert form



## Alpha DaRT

- The Alpha DaRT utilizes stainless steel sources that are impregnated with Radium-224
- When the Alpha DaRT source is injected into the tumor, the radium remains attached to the source while its daughter atoms detach, emitting cytotoxic alpha particle payloads as they move deeper into the tumor until eventually stabilizing

Alpha DaRT is designed to overcome the range limitations of alpha particles through precise release of alpha emitters into the tumor, generating a potent and tight distribution of alpha radiation

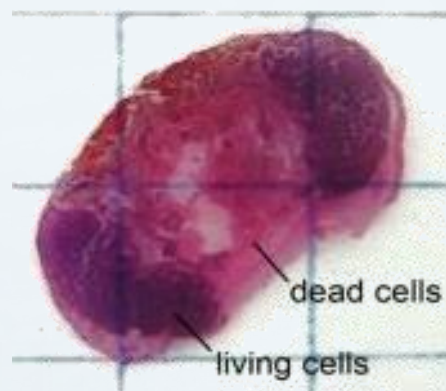
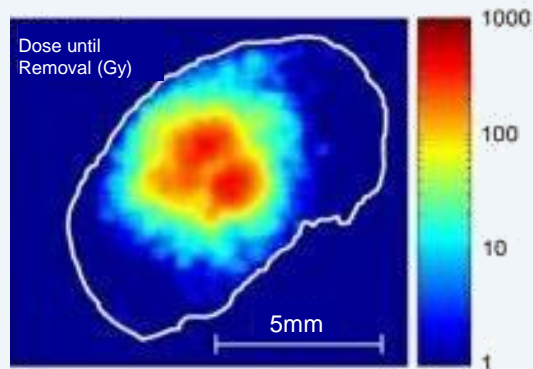
# Alpha DaRT - Diffusing Alpha-emitters Radiation Therapy

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<https://www.youtube.com/watch?v=nwfzJHm0fTQ>

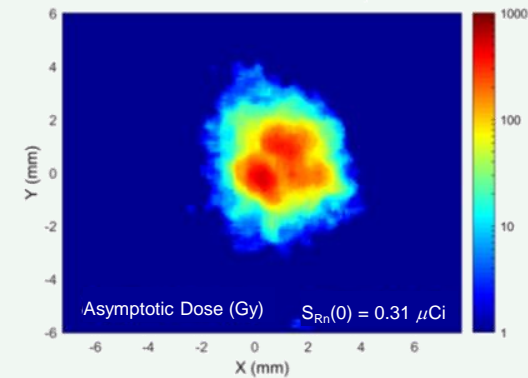
# Alpha DaRT Has a Unique Potential to Preserve Healthy Tissues

Alpha DaRT is unique in its potential to deliver a high dose of radiation in a very conformal form, with sharp dose drop-off outside of a 5mm range

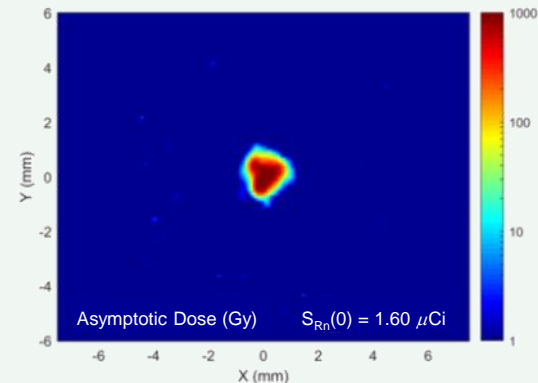


The range of the Alpha DaRT was observed to be meaningfully more extensive in tumor tissue than in healthy tissue in animal studies

Diffusion in SCC

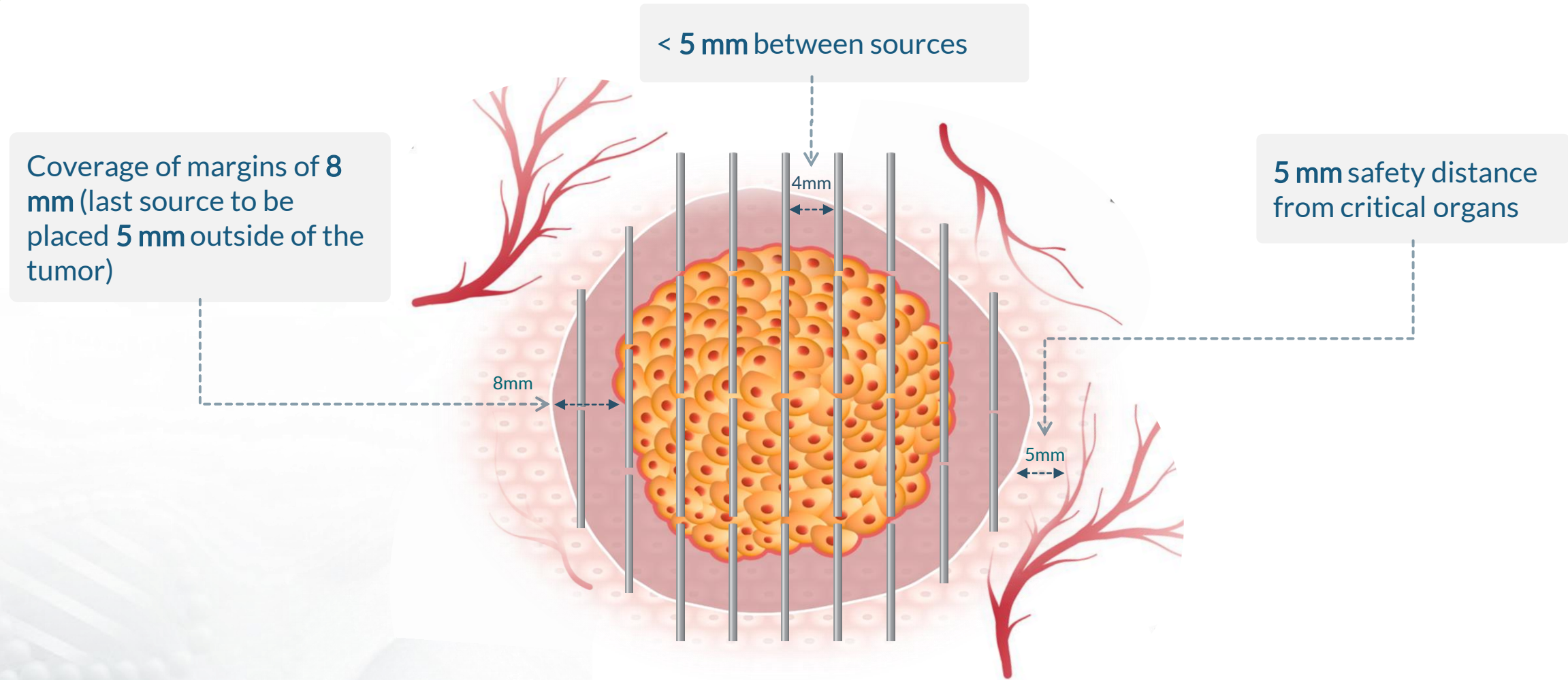


Diffusion in healthy tissue



# Alpha DaRT Source Placement

Through a series of Alpha DaRT injections to the tumor, spread a few millimeters apart, a clinician can potentially deliver alpha radiation to the full geometry of the tumor while taking care to avoid sensitive healthy tissue around the tumor



# Our Applicators Allow Delivery Into Both Superficial & Internal Tumors

We Have a Total of Seven Applicators Which Have Been Developed for a Range of Potential Uses to Accommodate for:

Treatment delivery method

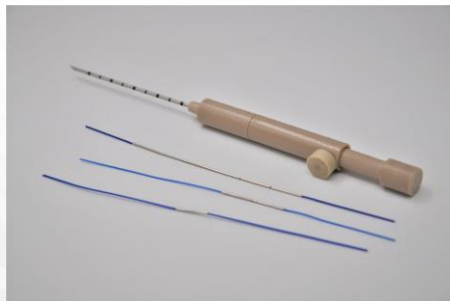
Duration of implantation

Tumor Location

## Temporary Implants (Superficial Tumors)

*Applicators are supplied preloaded, sealed and designed for immediate use*  
*Sources are hollow and strung onto a surgical suture, allowing the clinician to insert the sources into the tumor and leave the suture in place*

Alpha DaRT Needle Applicator



Needle Applicator in Action



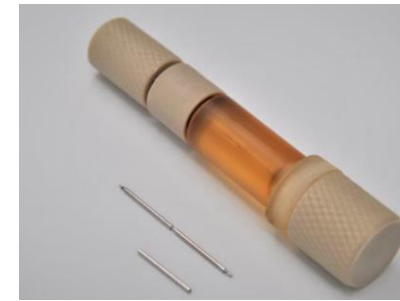
**Example Indication: Superficial Tumors.**

*sources are affixed to a biocompatible suture and loaded inside the needle*

## Permanent Implants (Internal Tumors)

*Applicators are designed to allow clinicians flexibility to receive the sources preloaded, or load the sources in the course of treatment, and to select how many sources to deliver*

Loading Device



Procedure: FNA in Conjunction with Endoscopic Ultrasound



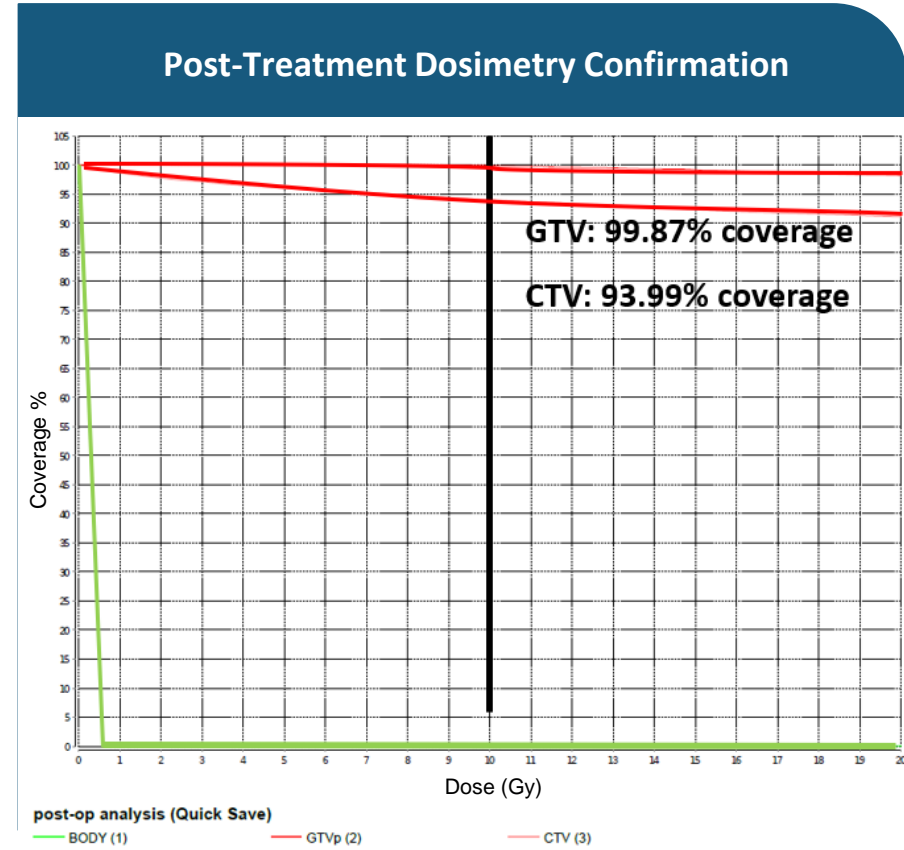
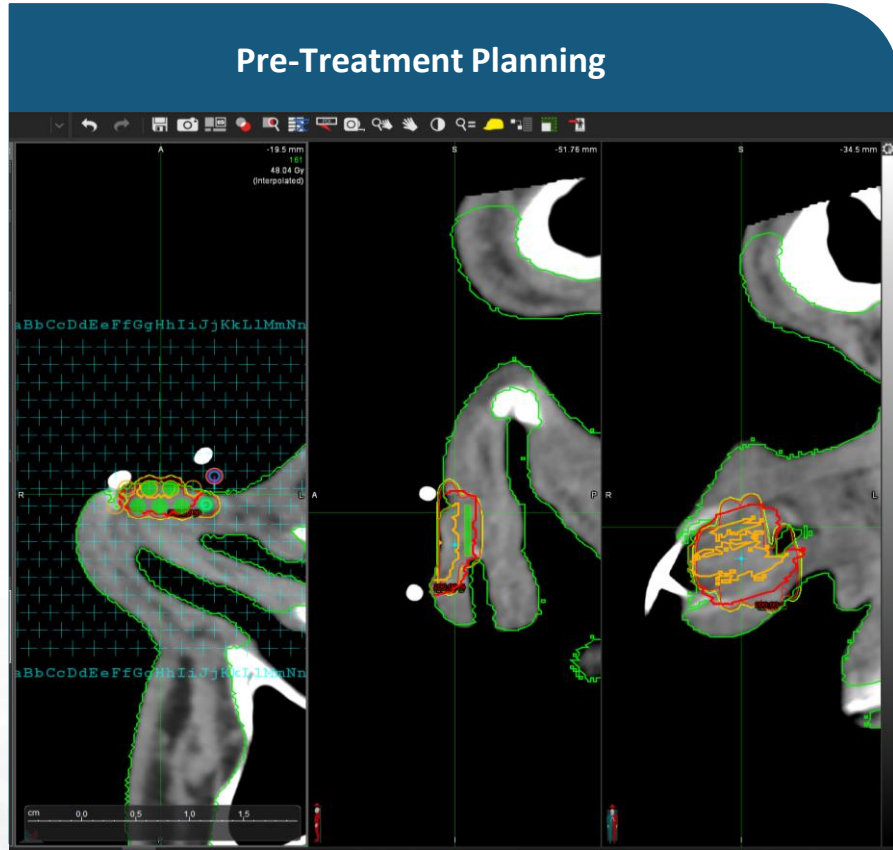
**Example Indication: Pancreatic Tumors.**

*Device is designed to be fitted to existing needles such as standard Fine Needle Aspirator (FNA) to ultimately deliver sources into the tumor*

# Treatment Planning in Partnership with MIM Software



Treatment planning software may serve to increase the precision and robustness of Alpha DaRT use, by allowing the clinician to calculate the alpha-specific dosimetry for the desired plan before treatment, and then check the tumor coverage post treatment



Alpha Tau has announced an agreement with MIM Software for continued collaboration on Alpha DaRT treatment planning, including development of new features and support for the Alpha DaRT across multiple potential indications, integration into all clinical trials involving the Alpha DaRT, and bundling the MIM software with the Alpha DaRT for future commercial sales.



Preclinical Data

**Demonstrated Local and Immune Responses  
Across a Variety of Tumor Types in Animal  
Models**

# Response Observed in All Tested Solid Tumors in Preclinical Studies

23 Published Preclinical Studies in Peer-Reviewed Journals

Across a variety of tumor types, we have not observed resistance to the radiation delivered by the Alpha DaRT

Squamous Cell Carcinoma

Colon Carcinoma

Lung Adenocarcinoma

Glioblastoma Multiforme

Lung Squamous Cell Carcinoma

Sarcoma

Pancreas Adenocarcinoma

Melanoma

Prostate Adenocarcinoma

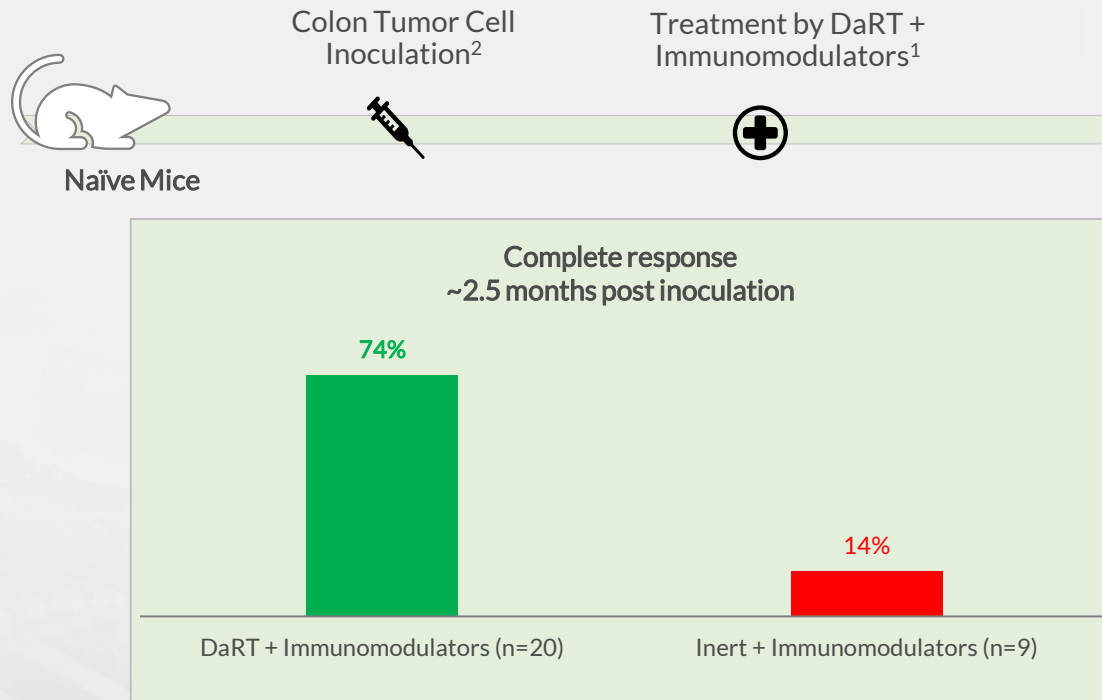
Breast Carcinoma



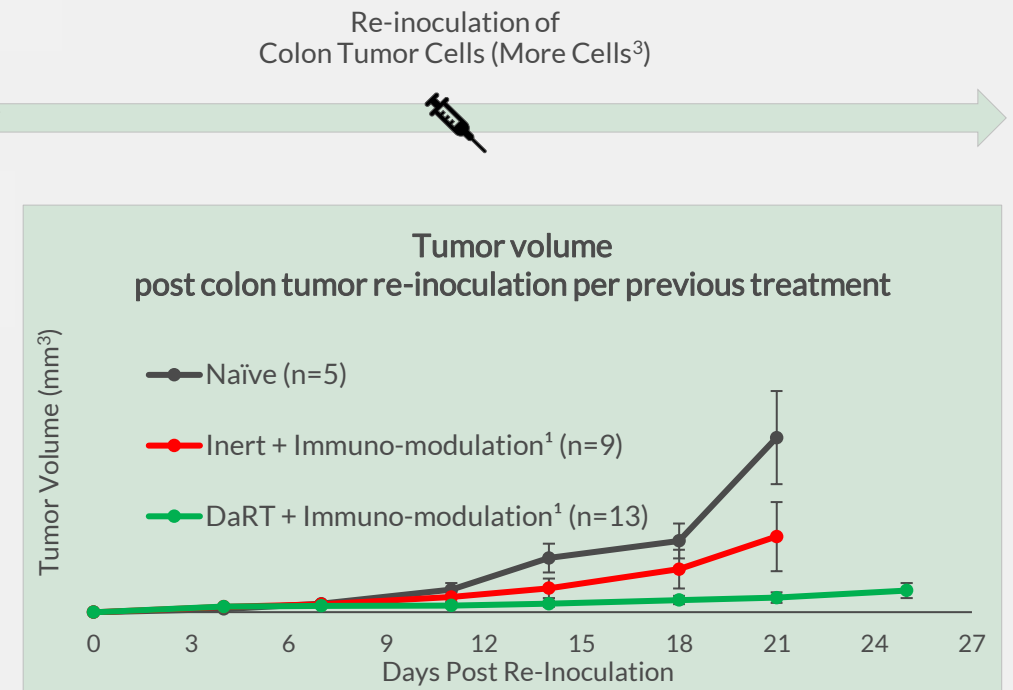
# Observed Cancer-Specific Immune Protection (1/2)

In challenging mice 4 months after treatment, those previously treated by the Alpha DaRT displayed a meaningful retained protection against regrowth of the same tumor type, as compared to the two control groups

## Tumor Treatment by DaRT + Immunomodulators<sup>1</sup>



## Tumor Re-Inoculation after Treatment by DaRT + Immunomodulators vs. Inert<sup>1</sup>

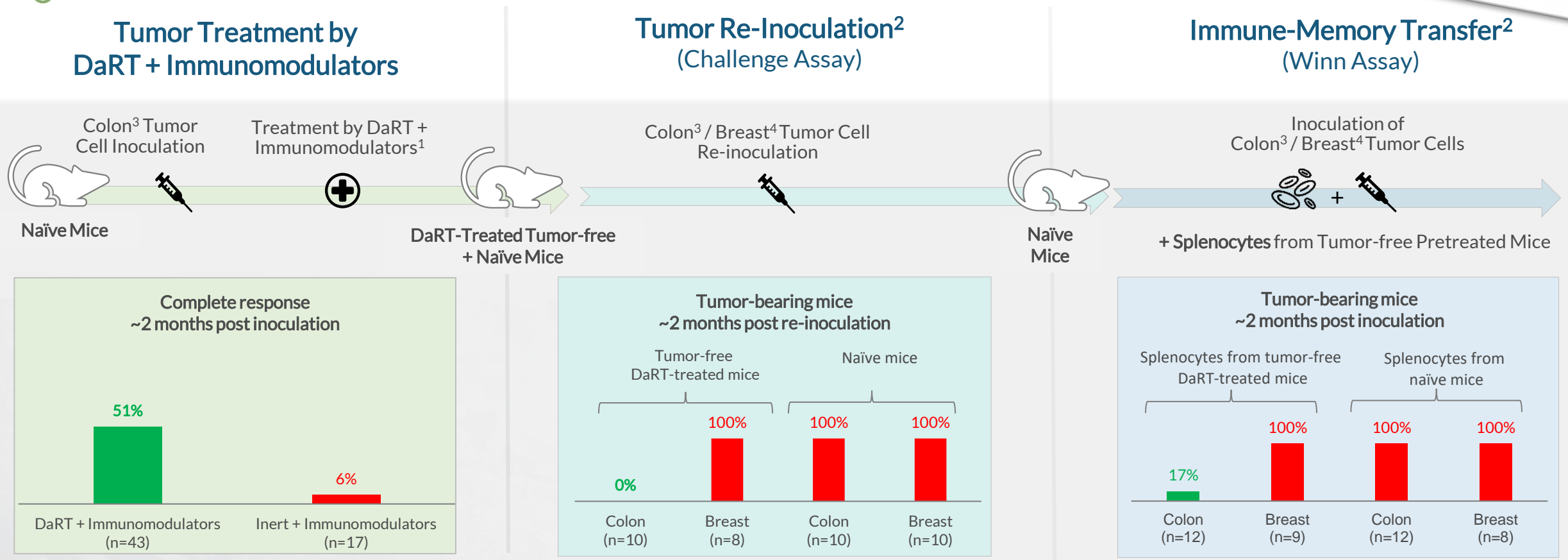


(1) Three groups of mice were inoculated with  $5 \times 10^5$  CT26 tumor cells and then treated with (1) DaRT + CP, Sildenafil and 2xCpG, N=10 (2) DaRT + CP, Sildenafil and CpG, N=10 or (3) inert + CP, Sildenafil and 2xCpG, N=9. Complete responders or tumor-resected mice were re-challenged ~4 months after DaRT with  $5 \times 10^6$  CT26 tumor cells.  
 (2)  $CT26 \ 5 \times 10^5$ .  
 (3)  $CT26 \ 5 \times 10^6$ .

# Observed Cancer-Specific Immune Protection (2/2)

This activity was then shown to be tumor-specific – the challenge only resisted regrowth of the same tumor line. It was also shown to be transferrable via the transfer of splenocytes

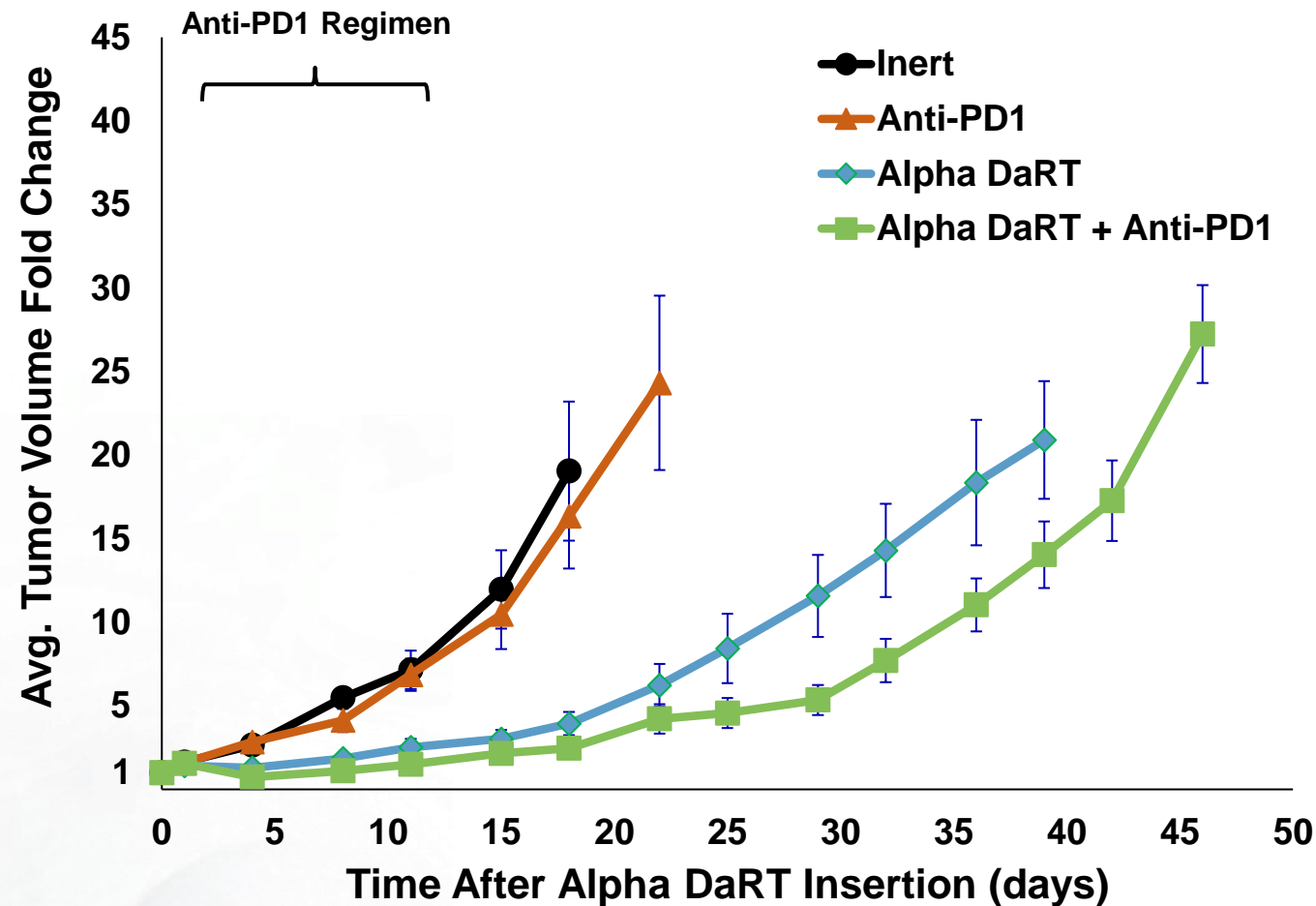
Combining alpha radiation-based brachytherapy with immunomodulators promotes complete tumor regression in mice via tumor-specific long-term immune response  
 Vered Domankevich, Adi Cohen, Margalit Efrati, Michael Schmidt, Hans-Georg Rammensee, Sujit S. Nair, Ashutosh Tewari, Itzhak Kelson & Yona Keisari



(1) Immuno-modulation refers to a combination of low dose CP, Sildenafil and CpG.  
 (2) Mice with CR from DaRT + immuno-modulators (n = 18) and naive mice (n = 20) were inoculated with 5 x 10<sup>5</sup> CT26 or DA3 cells 52 days post inoculation (Challenge Assay). Naive mice were injected intradermally with splenocytes from either naive or CT26-bearing mice treated by DaRT and immunomodulators, coupled with CT26 or DA3 tumor cells (Winn assay). The presented results are based on cumulative data from two different experiments.  
 (3) CT26 5 x 10<sup>5</sup>.  
 (4) DA3 5 x 10<sup>5</sup>.

# Alpha DaRT Elicits Effect from anti-PD1 in SCC Mouse Model (SQ2)

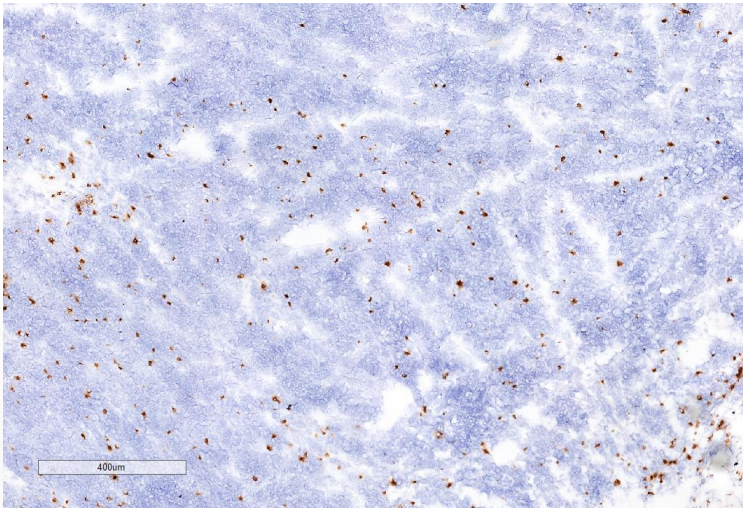
While mice with the SQ2 squamous cell carcinoma model showed little to no effect when treated with a murine anti-PD1 agent, the observed effect was larger for the combination with Alpha DaRT than for Alpha DaRT on its own



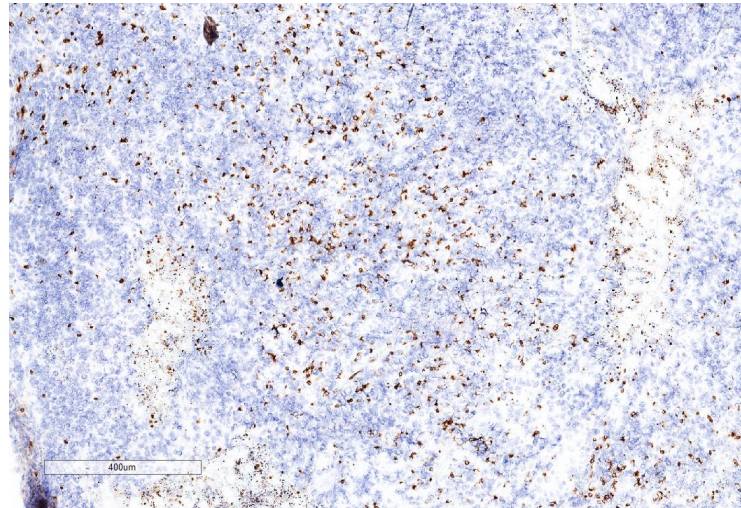
# Alpha DaRT Increases Infiltration of CD3+ T-cells Into the Tumor

The combination of Alpha DaRT with anti-PD1 demonstrates the highest level of TILs in mice with SQ2 SCC tumors, potentially indicating an ability to potentiate the checkpoint blockade

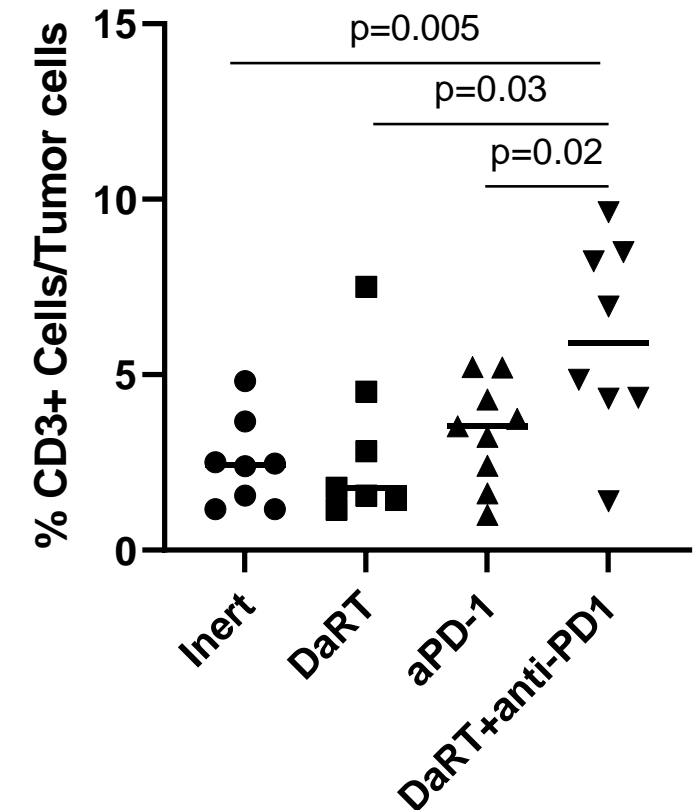
anti PD-1



Alpha DaRT + anti PD-1



**TILs in SQ2 tumors**



Clinical Data

## Encouraging Results Across a Variety of Solid Tumor Types

# Outline of Our First Clinical Study: Skin / Head & Neck SCC

*Trial Sites: Israel, Italy*

Primary objective: Evaluate feasibility & safety

Secondary objective: Evaluate initial tumor response & local progression-free survival

## Key Eligibility Criteria



**SCC** histopathologically confirmed

**Lesions**  $\leq 5$  cm\*

**Age**  $\geq 18$

**ECOG performance scale**  $\leq 2$

**Patients** W/O immunosuppression

Generally **previously treated by radiation or surgery, recurrent**

## Treatment & Procedure



**Treatment plan** based on CT-simulation

**Sources** 1cm length, 0.7mm diam.

**Activity per source** 2  $\mu$ Ci

**Outpatient** setting

**Local** anesthesia

**Number of sources** inserted: min 3, max 169

## Timeline and Follow-Up



**Alpha DaRT** sources insertion

**Removal** after 15 days

**Check-up** on days 4, 9 and 30 after insertion

**Long term** follow up based on standard of care

\*in the longest diameter (without nodal spread).



# Skin / Head & Neck SCC Study Results



100% overall response rate



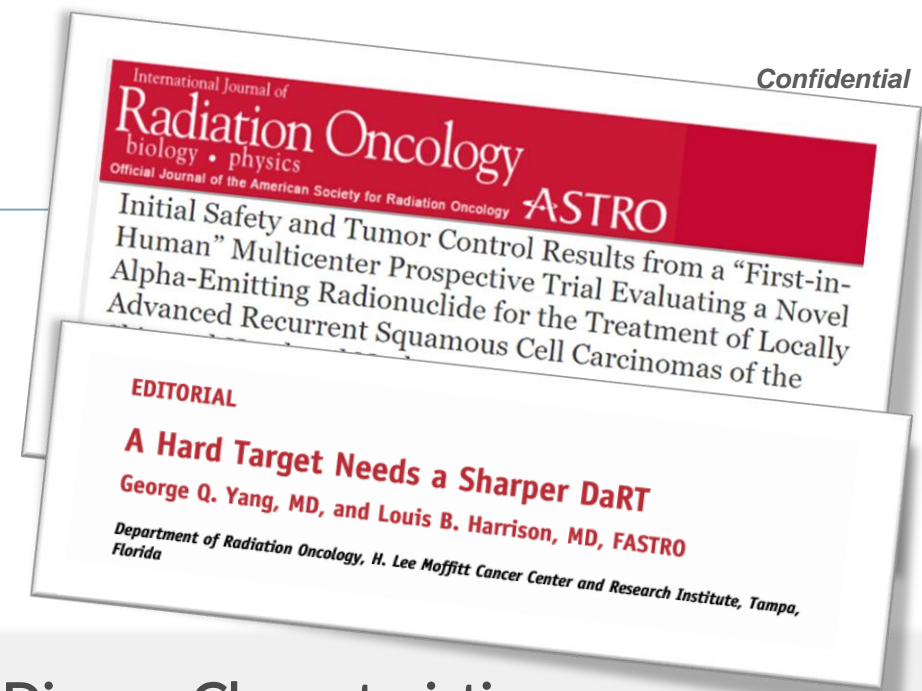
Durable responses observed



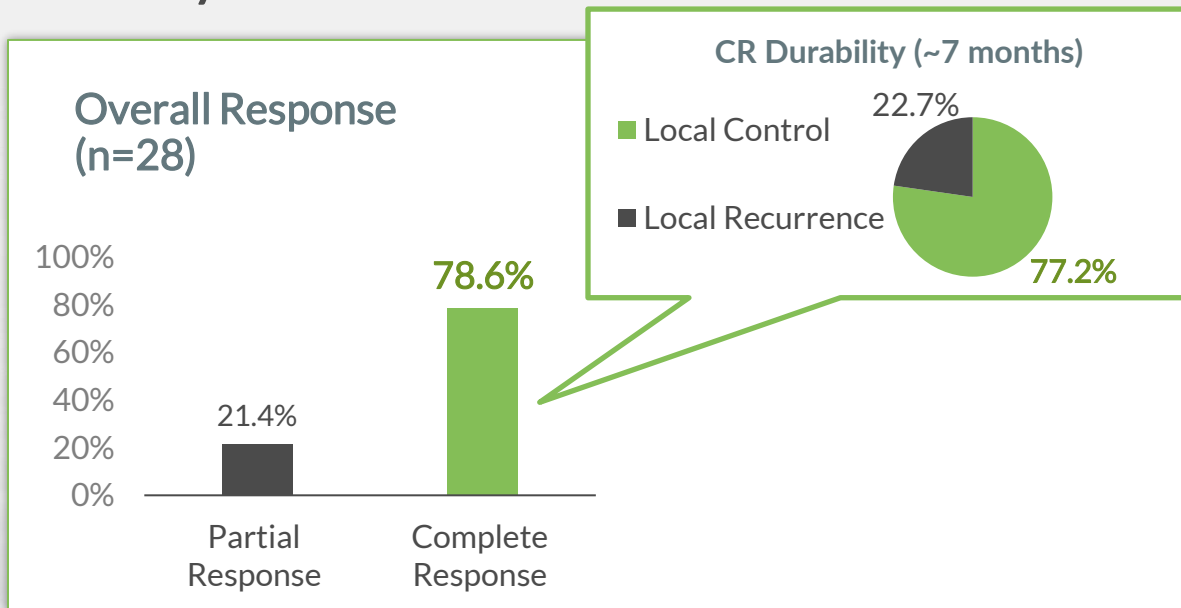
Responses observed within days



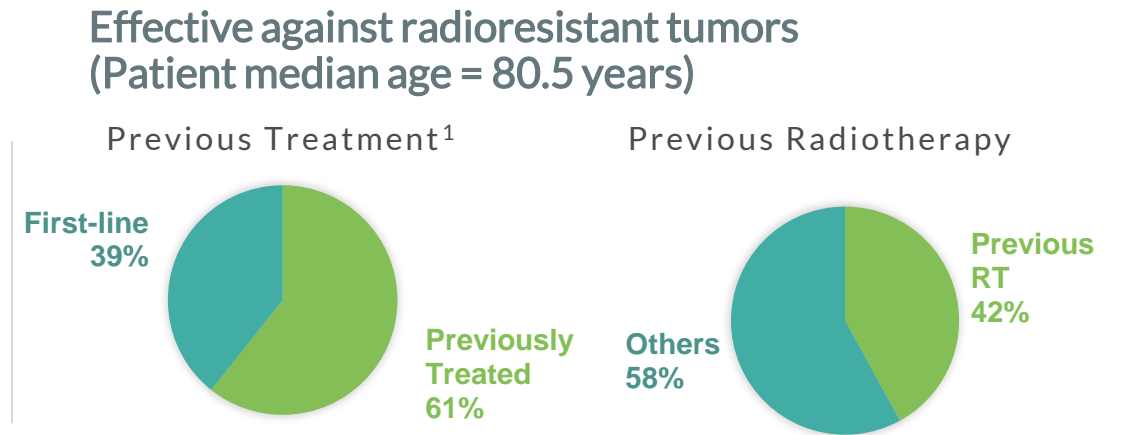
Well tolerated; no systemic toxicity observed



## Efficacy Results



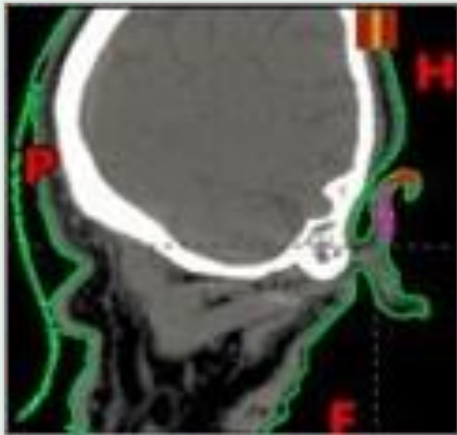
## Baseline Disease Characteristics



<sup>1</sup>Most patients (60.7%) had recurrent and previously treated disease by either surgery, prior external beam radiotherapy or both; 13 of 31 (42%) had received prior RT.

# AP-02 Complete Response

Age	80	Applicators used	6
Previous treatments	Radiation, Surgery	Alpha DaRT sources inserted	10
Tumor initial volume [cm <sup>3</sup> ]	1.4	Total activity [μCi]	20



**Planning**



**Before**  
21-Mar-2017



**During**  
21-Mar-2017



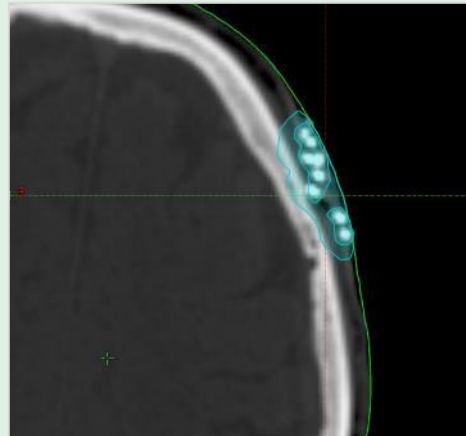
**After**  
01-Jun-2017

# AP-022 Complete Response

Age	68	Applicators used	12
Previous treatments	None	Alpha DaRT sources inserted	24
Tumor initial volume [cm <sup>3</sup> ]	1	Total activity [μCi]	48



**Before**  
27-Aug-2018



**During**  
30-Aug-2018



**During**  
30-Aug-2018



**After**  
30-Sep-2018

# Alpha DaRT Treatment was Well Tolerated

No systemic toxicities and minimal ( $\leq$  grade 2) local toxicities observed to date



## Targeted treatment

Designed to spare neighboring healthy tissue



## No systemic toxicity observed

Negligible and short-term radioactivity in the patient's body



## Minimal local toxicity observed

Minimal local toxicity with grade  $\leq 2$  resolved within a month



## Safe procedure for caregivers

No special shielding required



## No suppression of immune system observed

Critical in times of pandemic

Acute Local Toxicity	Incidence (%)		
	Severity Grade		
	1	2	3
Administration site erythema	11 (41%)	9 (33%)	0 (0%)
Administration site edema	9 (33%)	10 (37%)	0 (0%)
Administration site pain	8 (30%)	11 (41%)	0 (0%)
Administration site exudate	2 (7%)	8 (30%)	0 (0%)
Administration site ulcer	4 (15%)	5 (19%)	0 (0%)
Administration site numbness	1 (4%)	0 (0%)	0 (0%)
Administration site pruritus	3 (11%)	0 (0%)	0 (0%)
Administration site bleeding	1 (4%)	0 (0%)	0 (0%)
Aural myiasis (administration site)	1 (4%)	0 (0%)	0 (0%)
Decreased appetite	1 (4%)	0 (0%)	0 (0%)

# Potential Systemic Immune Effect Observed in One Patient Where a Second, Untreated Lesion Manifested CR

✔ Complete Response + Potential Systemic Immune Effect



## Treated Tumor

Before

30-Nov-17



After

29-Dec-17



## Untreated Tumors

Before

30-Nov-17



After

29-Dec-17



# U.S. Pilot Feasibility Study – Trial Design

FDA Breakthrough Device Designation received in June 2021



Locations	5 centers in the US, led by Memorial Sloan Kettering Cancer Center
Treatment Timeframe	H2 2021
# of Patients	10
Tumor Type	Skin Cancers
Primary Objectives	Determine feasibility of delivering radiotherapy using Alpha DaRT, with successful delivery in at least 7 patients, and assess frequency and severity of acute AEs
Secondary Objectives	Assessments of radiotherapy-related AEs, tumor response, radiation safety, stability of device placement, and QoL
Eligibility	Malignant skin or superficial soft tissue tumor 1-5 cm in size that is suitable for percutaneous interstitial brachytherapy

# Case Study - 77 Y/O with Recurrent BCC on the Nose



Prior treatments: Surgery (2005)

## Tumor Size:

Longest diameter 1.59 cm

Depth 0.5 cm

Volume 0.65 ml

## Alpha DaRT Treatment:

Applicators used 15

Alpha DaRT sources inserted 20

Total activity [ $\mu$ Ci] 40

# Case Study - 77 Y/O with Recurrent BCC on the Nose

## Results



**Simulation Day**



**Insertion Day**



**Removal Day**  
15 days



**Complete Response**  
12 weeks



# U.S. Pilot Feasibility Study – Safety Results

- Twenty-two (22) **total adverse events (AEs)** were reported in 7 subjects
- Most AEs were of **mild or moderate severity**
- Two (2) serious AEs (SAEs) in a single subject – **both not related to study device or procedure**

## Number of Subjects with Procedure- or Device-Related\* Adverse Events by Severity Grade

Adverse Event	Severity Grade		
	1	2	3
Dermatitis radiation	2	1	0
Localized edema	1	0	0
Joint range of motion decreased	0	1	0
Pain	0	1	0
Pruritis	2	0	0
Wound infection	0	1	0

Note: Adverse events are presented according to CTCAE V5 coded terms.

\* Probably or possibly related

# U.S. Pilot Feasibility Study – Efficacy Results

---

-  All 10 subjects achieved a **complete response (CR)** at the 12-week follow-up visit
-  There were **no reported relapses** of disease by the final study visit at 24 weeks

# Impressive Efficacy & Safety Data Collected in Long-Term Follow-Up

## Data Set Description

Data collected from four feasibility trials in unresectable, recurrent, or locally advanced head and neck or skin cancers

81 treated lesions in 71 patients

Median follow-up of 14 months  
(range: 2-51 months)

## Efficacy



- ✓ 89% of treated lesions achieved complete response (CR)
- ✓ 77% two-year local recurrence-free survival (LRFS)

## Safety

- ✓ ~20% of patients had acute grade 2 toxicities and no patients had acute grade 3 or higher toxicities
- ✓ No grade 2 or higher late toxicities observed 6 months post-treatment

Short-term local responses led to durable long-term control in difficult-to-treat tumors

# Outline of Our Multicenter Pivotal Recurrent SCC study

-  **Primary / safety objectives:**
  - ORR based on Best Overall Response
  - DOR 6 months after initial response
  - Assess the safety based on statistics of device-related AEs (per CTCAE v5)
-  **Secondary objectives:** Evaluate O-DOR, local control, PFS and OS (all up to 12 months), and QoL Metrics

## Key Eligibility Criteria



**Recurrent** non-metastatic cutaneous **SCC**

Patient with **no curative standard-of-care options**

No **previously untreated SCC**

**Sample size** N = 86 patients

## Treatment and Procedure



**Treatment plan** based on CT-simulation

**Sources** 1cm length, 0.7mm diam.

**Activity per source** 3  $\mu$ Ci

**Local** anesthesia

**20 U.S. sites** including UCLA, Emory University, Mayo Clinic, etc.

## Timeline and Follow-Up



**Alpha DaRT** sources insertion

**Removal** after 14 to 21 days

Weekly **follow-up** during the treatment period

# Focus on Internal Organ Treatments

We continue to make progress across internal organ indications, with multiple indications in large animal testing and/or in the stage of regulatory protocol submission for upcoming clinical trials, expanding from Israel to elsewhere in the world.

## Internal Organs in Focus



- Prostate – in Human Clinical Trial
- Pancreas – in Human Clinical Trial
- Brain – GBM + Brain Mets
- Liver
- Breast
- Lungs
- Rectum



Internal Organs

**A Feasibility and Safety Study of Intratumoral  
Diffusing Alpha Radiation Emitters on  
Advanced Pancreatic Cancer**  
AT-PANC-101

# Outline of the Pancreas Pilot Study in Canada

-  **Primary objective:** Evaluate feasibility & safety of Alpha DaRT sources inserted into pancreas in terms of incidence of device related AEs & SAEs.
-  **Secondary objective:** Evaluate efficacy (radiological ORR and change in tumor markers), OS, stent durability, and QoL

## Key Eligibility Criteria

Locally **advanced (Stage II or III)** or **metastatic (Stage IV)** pancreatic adenocarcinoma

**Inoperable** pancreatic cancer because:

- **Unresectable**
- **Metastatic** disease
- Medically **unfit** for surgery

No **concomitant chemotherapy** or **immunotherapy**

**Sample size** N = 37 patients

## Treatment and Procedure

**Treatment plan** based on CT

**Sources** 0.7 mm in diameter and 10 or 20 mm in length

**Activity per source** 3  $\mu$ Ci

Source insertion using **endoscopic ultrasonography** under sedation

## Timeline and Follow-Up

**Alpha DaRT** sources insertion

**Check-up** on days 6, 15, 21, 35, 60 after insertion

**Follow-up duration** up to 2 years

**Limit of 1 patient / month for first 5 patients, to confirm safety**

# Canada Pancreas Trial Baseline Characteristics

Subject ID	Age (years)	Sex	ECOG Score	Tumor Stage	Tumor Location	Pancreatic Cancer Inoperability	Prior Treatments	Length of Alpha DaRT Sources (cm)	GTV Coverage @ 16 Gy Alpha Radiation Dose
PANC-101-02-001	78	M	1	Stage IV	Pancreatic head/uncinate	Metastatic disease	Chemotherapy: Gemcitabine and Paclitaxel; Gemcitabine	3	8%
PANC-101-02-002	68	F	2	Stage III	Pancreatic head	Unresectability	Chemotherapy: FOLFIRINOX (fluorouracil+leucovorin+oxaliplatin+irinotecan); Gemcitabine and Paclitaxel	11	13%
PANC-101-02-003	69	F	0	Stage II	Pancreatic head/neck	Unresectability	Chemotherapy: FOLFIRINOX; Abraxane and Gemcitabine	21	44%
PANC-101-02-004	84	F	1	Stage IV	Pancreatic head	Metastatic disease	Chemotherapy: Capecitabine	22	12.5%
PANC-101-02-005	71	F	0	Stage IV	Pancreatic neck	Metastatic disease	None	24	29.5%



# Safety and Feasibility Outcomes

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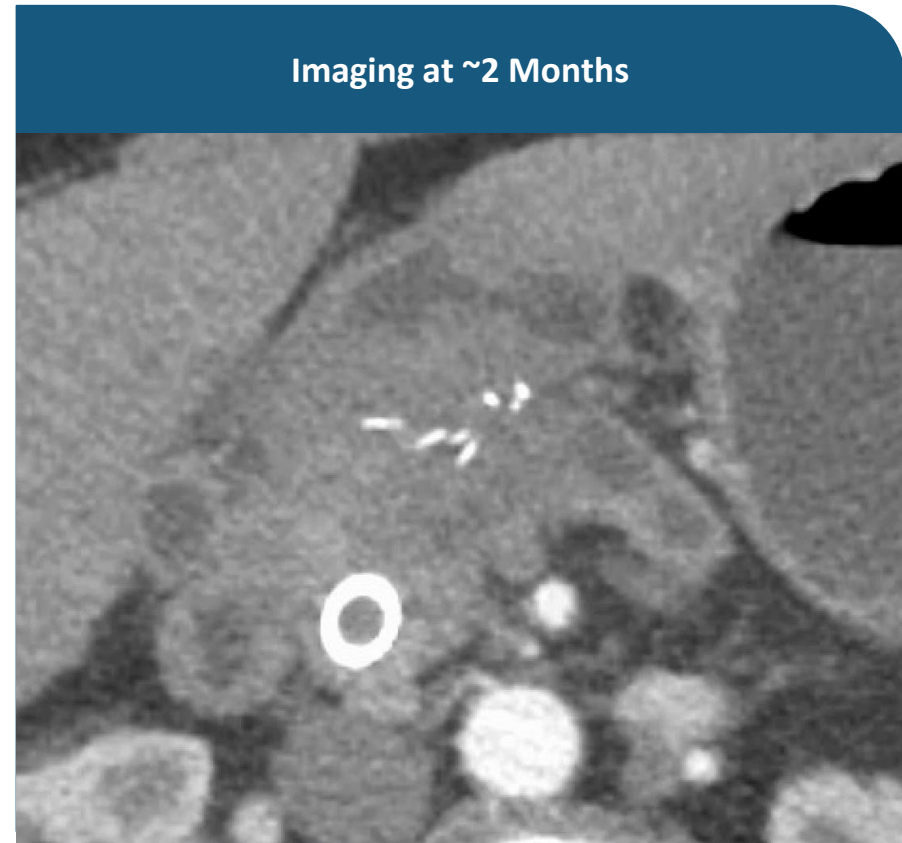
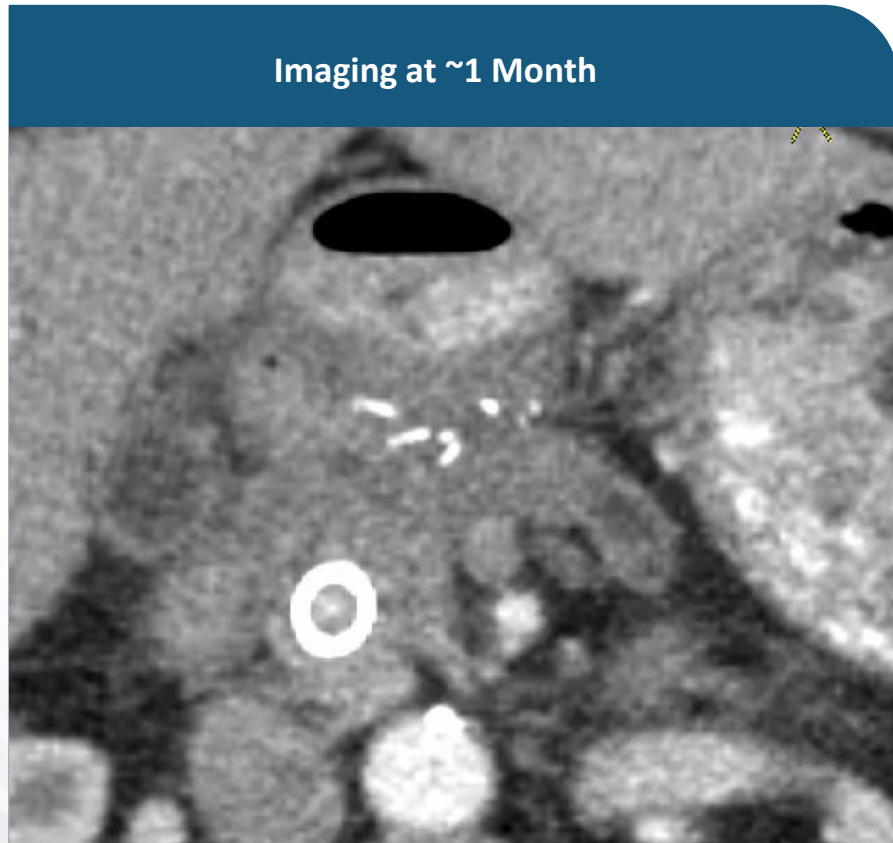
- ✔ Successful delivery to all 5 patients
- ✔ All patients were **discharged** from the hospital **on the same day** as the procedure
- ✔ All device- or procedure-associated adverse events (2) were **mild** (Grade 1)
- ✔ **No Grade 3** or higher associated events
- ✔ All SAEs were **not associated** with the Alpha DaRT or the procedure

# Early Response Data

Subject ID	Age (years)	Sex	ECOG Score	Tumor Stage	Tumor Location	Pancreatic Cancer Inoperability	Prior Treatments	Length of Alpha DaRT Sources (cm)	GTV Coverage @ 16 Gy Alpha Radiation Dose
Progressive Disease; Death ~3 months after treatment								3	8%
Progressive Disease; Death ~3 months after treatment								11	13%
Stable Disease at 28 days; Partial Response at 69 days								21	44%
Stable Disease at 28 and 98 days								22	12.5%
Stable Disease at 28 days								24	29.5%

# PANC-101-02-003 – Partial Response

Patient #3 in the trial demonstrated a partial response at 69 days after treatment, as can be seen below, while the Alpha DaRT sources appear to stay largely in place

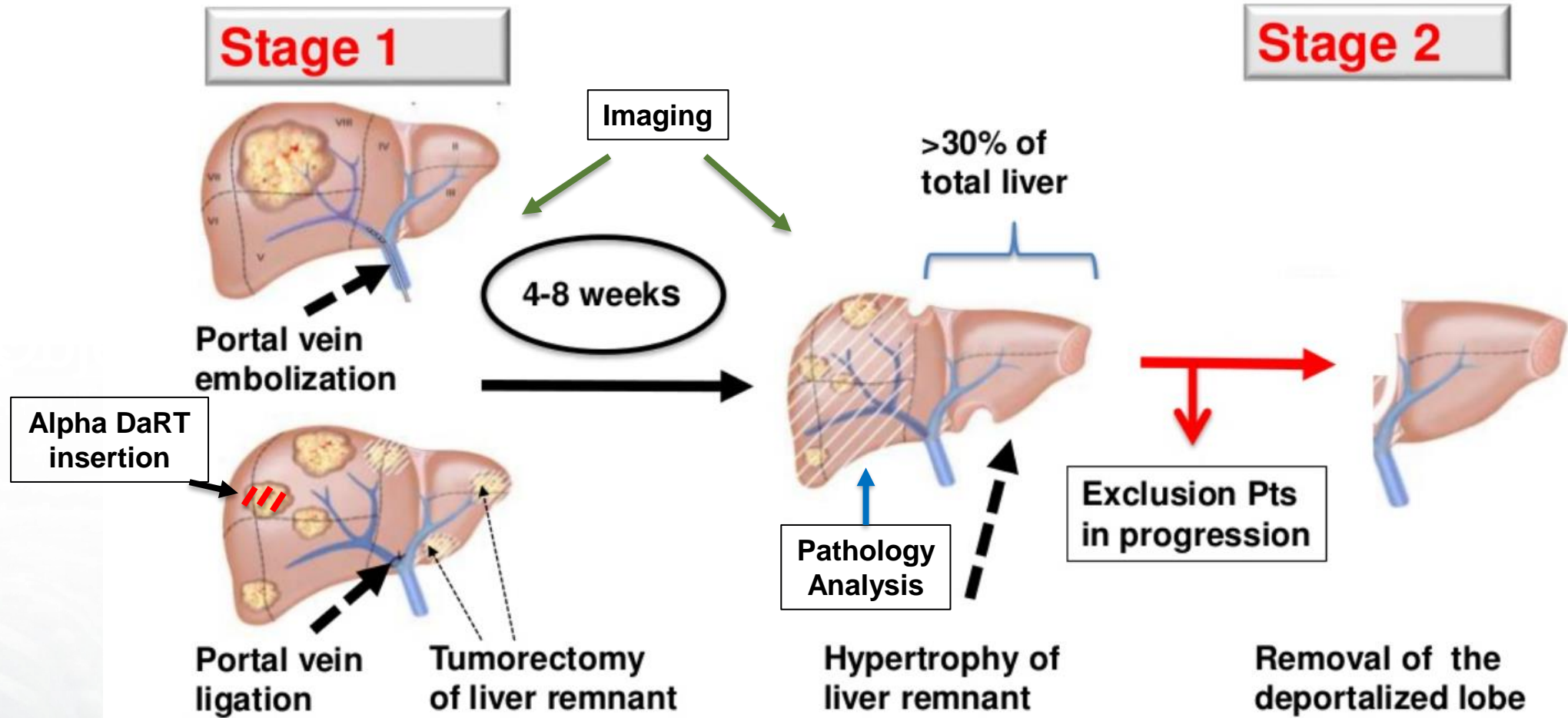


Internal Organs

**A Feasibility and Safety  
Study of Intratumoral Diffusing  
Alpha Radiation Emitters for the  
Treatment of Liver Metastases**  
CTP-LIV-00



# Study Schema

## Liver study



Clavien et al. Strategies for safer liver surgery. NEJM, 2017

# Outline of Liver Metastases Study

-  **Primary objectives:** Evaluate feasibility & safety of Alpha DaRT implanted in liver metastases
-  **Secondary / exploratory objectives:** Evaluate pathological and radiological response, determine immunological impact, stratify differences in response by histopath. growth patterns (vascular / immuno.)

## Key Eligibility Criteria



Referred for a **two-staged hepatectomy** to resect liver metastases of colorectal cancer

No prior use of **systemic investigational agents** for primary cancer

**Sample size** N = 10 patients

## Treatment and Procedure



**Treatment plan** based on CT scan or MRI

**Sources** 0.7 mm in diameter and 1 cm in length

**Activity per source** 3  $\mu$ Ci

**General** anesthesia

## Timeline



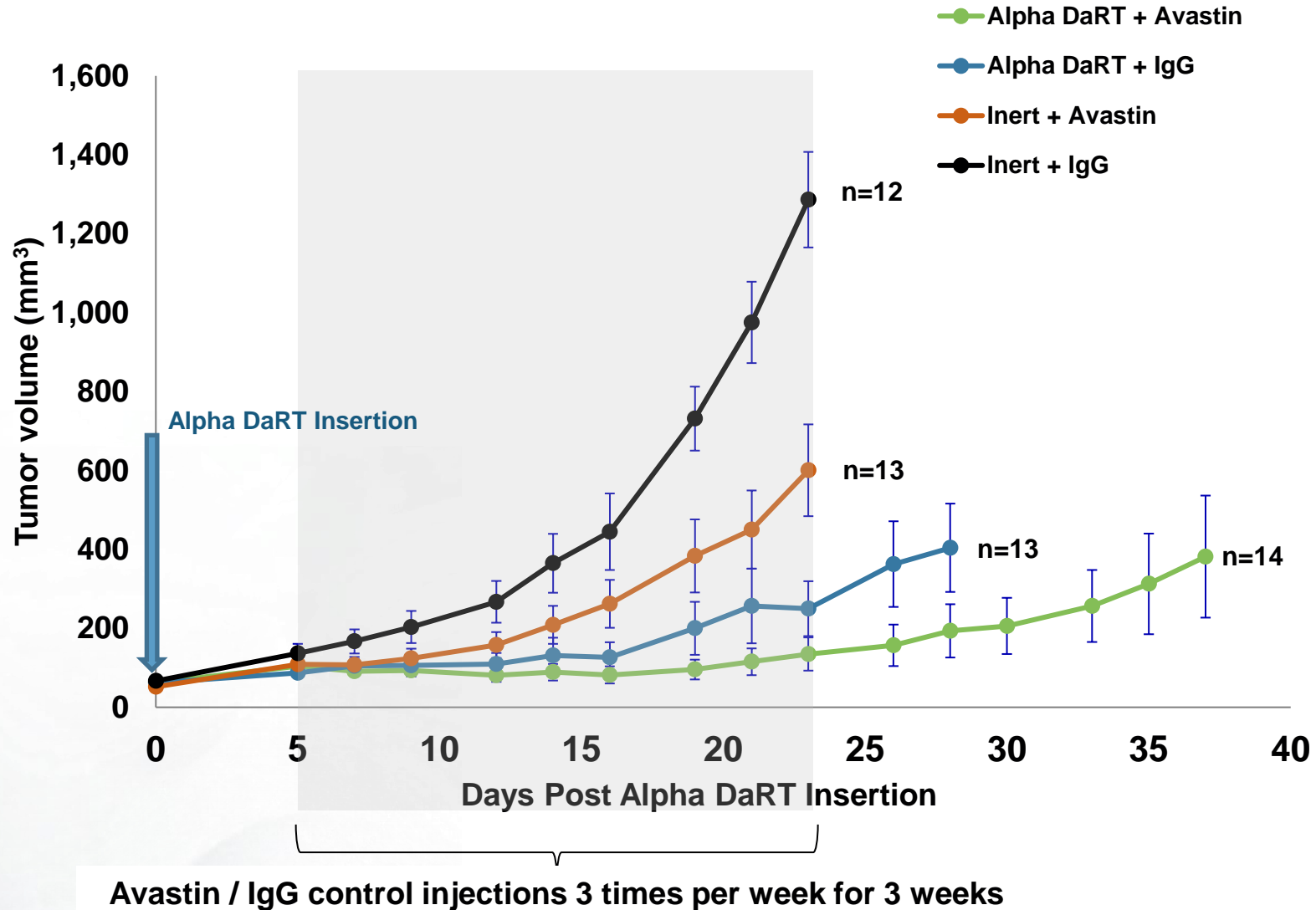
- 1<sup>st</sup> operation:** one side of the liver is cleared from its metastases & Alpha DaRT sources are implanted in the other side of the liver
- 3 - 4 cycles of **chemotherapy** (6 - 8 weeks)
- 2<sup>nd</sup> operation:** The liver lobe containing the metastasis with the sources is resected, to leave the patient with a disease-free liver



Internal Organs

## Glioblastoma Multiforme

# Alpha DaRT + Avastin Combo Showed Attenuated Growth of GBM Xenografts





# Radial Applicator Overview

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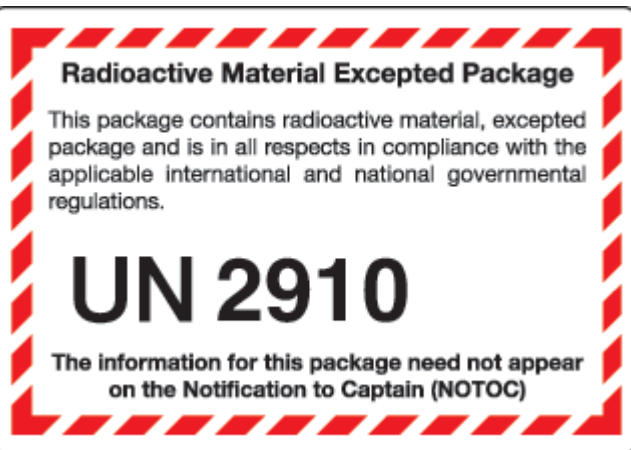
<https://www.youtube.com/watch?v=IJY965J0xMk>



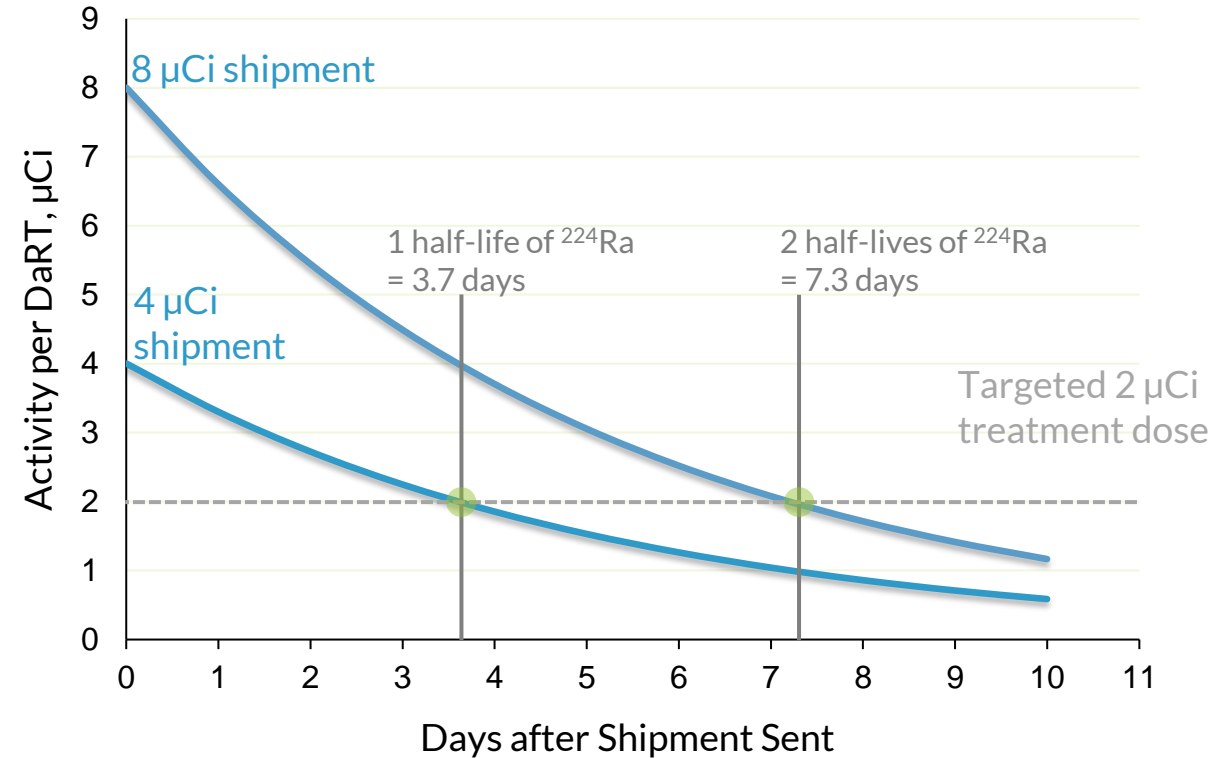
# Simple Radioactive Supply Chain

Delivery does not require any special handling and simple planning ensures on-time arrival

Alpha DaRT is shipped in Excepted Packages (low levels of radioactivity) or Type A packages, and may therefore be dispatched in suitable applicators by standard courier, requiring no special handling or protective gear in transit



## Alpha DaRT Radioactive Decay



**Personalized treatment, shipped out on a per-patient basis**  
Simple planning ensures that an Alpha DaRT arrives with the required amount of  $^{224}\text{Ra}$  available, even when allowing for radioactive decay, based on the known half-life of the  $^{224}\text{Ra}$

# Global Manufacturing Facilities

For efficient commercial operations, we look to establish manufacturing operations in multiple regions of the world, to enable relatively short shipping times to our core markets



Hudson, New Hampshire  
*(In Design)*



Jerusalem  
*(~400,000 sources per year - Ramping Up)*

Lawrence, Massachusetts  
*(~125,000 sources per year - Ramping Up)*



Jerusalem  
*(Land Granted - Facility in Planning)*



Togane, Japan  
*(In Design)*

# The Alpha Tau Executive Team

Strong management team with years of experience across the scientific and medical device space



**Uzi Sofer**  
CEO &  
Chairman

- Co-Founder and CEO of BrainsWay (NASDAQ: BWAY)
- Medical device development, regulation, financing



**Raphi Levy**  
Chief Financial  
Officer

- Former executive director in charge of healthcare investment banking in Goldman Sachs Israel



**Prof. Itzhak Kelson**  
Chief Physics  
Officer

- Co-inventor of DaRT technology
- Emeritus professor of physics (taught at Tel Aviv University, Yale University, Weizmann Institute etc.)



**Prof. Yona Keisari**  
Chief  
Scientific  
Officer

- Co-inventor of DaRT technology
- Professor of Immunology and Microbiology at Tel Aviv University, former NCI Post Doc Fellow



**Peter Melnyk**  
Chief  
Commercial  
Officer

- Former CEO of Fortovia Therapeutics
- Former Chief Commercial Officer at Novocure
- Former Neuroscience marketing director at Bristol-Myers Squibb



**Robert Den, MD**  
Chief Medical  
Officer

- Radiation oncologist and Associate Professor at Thomas Jefferson University Hospital
- Medical degree from Harvard Medical School



**Amnon Gat**  
Chief  
Operations  
Officer

- >20 years experience in medical devices and healthcare
- Marketing strategy specialist



**Ronen Segal**  
Chief  
Technology  
Officer

- >20 years of top leadership roles, including medical device industry
- Chairman of the BSMT Consortium

# Board of Directors

Diverse mix of cancer therapeutic, medical device and financial expertise providing value-added oversight and guidance to corporate leadership



**Uzi Sofer**  
CEO & Chairman



**Michael Avruch**  
Director



**Morry Blumenfeld**  
Director



**Meir Jakobsohn**  
Director



**Alan Adler**  
Director



**Ruth Alon**  
Director



**Dr. David M. Milch**  
Director

- Co-Founder and CEO of BrainsWay (NASDAQ: BWAY)
- Medical device development, regulation, financing

- Expert in financing and restructuring
- CEO & CFO experience

- Former managing director at GE Healthcare, CEO of Qescon Consultants, Founding partner of Meditech Advisors Management, director at Mako

- Founder of Medison Ltd.
- Represents Amgen, Biogen, etc. for the marketing and distribution of their products in international markets

- 14 Years at McKinsey
- Senior Partner Evergreen Venture Capital
- Chairman and CEO of Oridion until its sale to Covidien

- Former founder/chair, Israel Life Science Industry
- Former/current board/chair of multiple companies, e.g., Brainsgate, Vascular Biotech
- Former GP, Pitango VC

- Former HCCC Chairman
- Active medical investor
- MD from Harvard Medical School

Significant Industry Experience:



# Anticipated Milestones

Geography	Indication	1H 2024	2H 2024	1H 2025	2H 2025
North America	Recurrent Cutaneous SCC (United States)		Completion of multi-center pivotal trial recruitment	Potential FDA submission	
	Pancreatic Cancer (Canada)		Completion of pilot trial recruitment		
	Liver Metastases (Canada)	First patient in feasibility trial			
Israel	Brain Cancer (GBM or Metastases)		First patient treated		
	Lung Cancer	First patient in feasibility trial			
Japan	Head & Neck Cancer		Potential PMDA approval		

Clinical / Enrollment

Regulatory

# Financial Position

✓ Public Since Mar-2022 (NASDAQ:DRTS)

✓ \$84.9mm in Cash & Deposits at YE 2023

✓ 2+ Years of Cash Runway



# AlphaTAU

## Saving Lives Globally





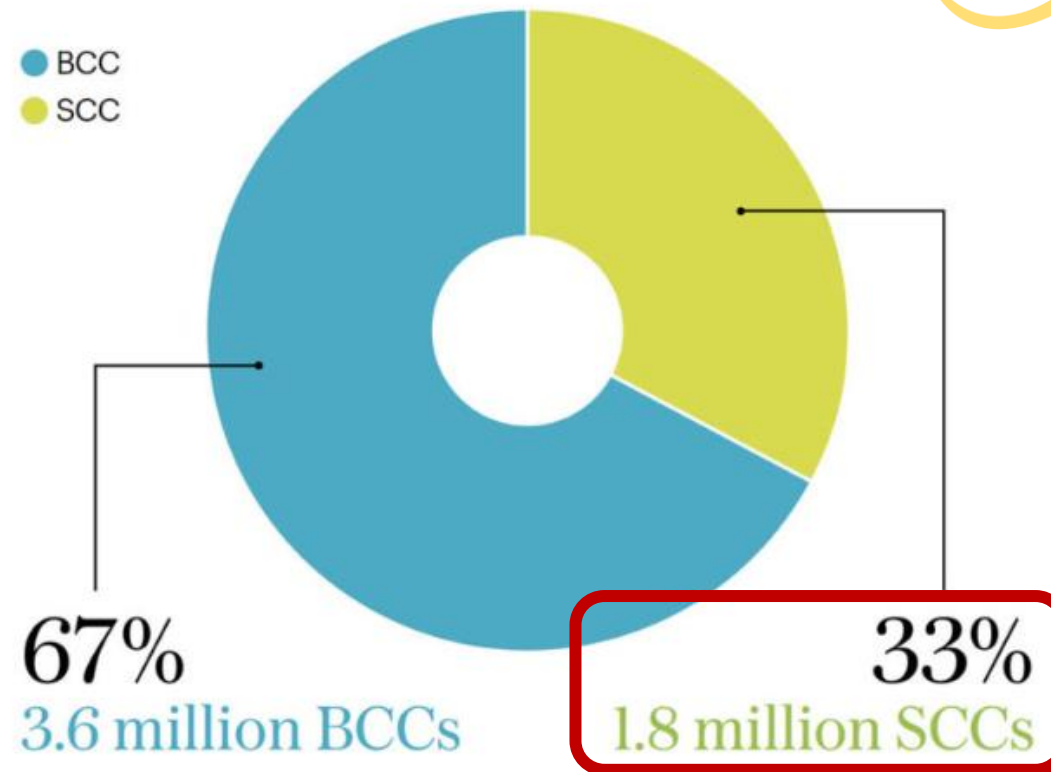
Appendix

# Analysis of U.S. Market Opportunity in Cutaneous Squamous Cell Carcinoma

# U.S. Annual Cutaneous Squamous Cell Carcinoma Incidence

Our New Approach to a Challenging Skin Cancer Statistic

BY SKIN CANCER FOUNDATION • APRIL 1, 2021



As of 2021

# Risk Stratification Per NCCN Guidelines



## NCCN Guidelines Version 1.2023 Squamous Cell Skin Cancer

[NCCN Guidelines Index](#)  
[Table of Contents](#)  
[Discussion](#)

STRATIFICATION TO DETERMINE TREATMENT OPTIONS AND FOLLOW-UP FOR LOCAL CSCC BASED ON RISK FACTORS FOR LOCAL RECURRENCE, METASTASES, OR DEATH FROM DISEASE

Risk Group <sup>a</sup>	Low Risk	High Risk	Very High Risk
Treatment options	<a href="#">SCC-2</a>	<a href="#">SCC-3</a>	<a href="#">SCC-3</a>
<b>H&amp;P</b>			
Location/size <sup>b</sup>	Trunk, extremities ≤2 cm	Trunk, extremities >2 cm – ≤4 cm Head, neck, hands, feet, pretibia, and anogenital (any size) <sup>e</sup>	>4 cm (any location)
Clinical extent	Well-defined	Poorly defined	
Primary vs. recurrent	Primary	Recurrent	
Immunosuppression	(-)	(+)	
Site of prior RT or chronic inflammatory process	(-)	(+)	
Rapidly growing tumor	(-)	(+)	
Neurologic symptoms	(-)	(+)	
<b>Pathology (<a href="#">SCC-A</a>)</b>			
Degree of differentiation	Well or moderately differentiated		Poor differentiation
Histologic features: Acantholytic (adenoid), adenosquamous (showing mucin production), or metaplastic (carcinosarcomatous) subtypes	(-)	(+)	Desmoplastic SCC
Depth <sup>c,d</sup> : Thickness or level of invasion	<2 mm thick and no invasion beyond subcutaneous fat	2–6 mm depth	>6 mm or invasion beyond subcutaneous fat
Perineural involvement	(-)	(+)	Tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring ≥0.1 mm
Lymphatic or vascular involvement	(-)	(-)	(+)

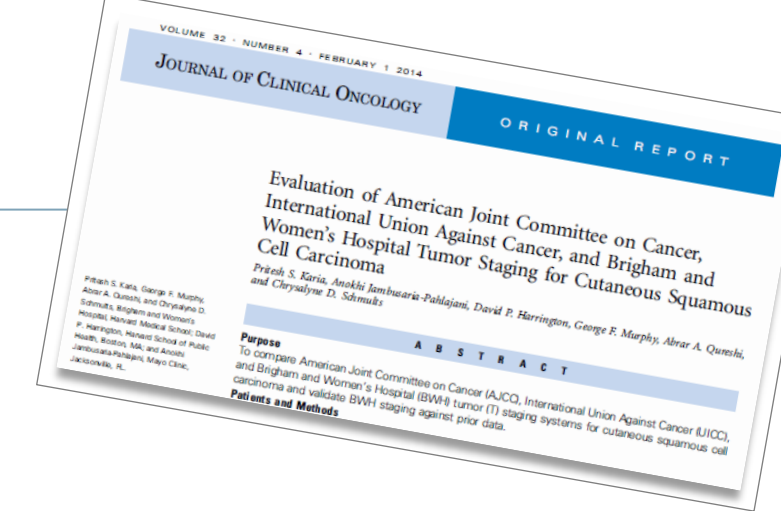
**Focus Patients**

Source: NCCN Guidelines for Cutaneous SCC: [https://www.nccn.org/professionals/physician\\_gls/pdf/squamous.pdf](https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf)

# How Many Are “High/Very-High Risk”?

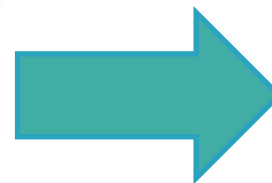
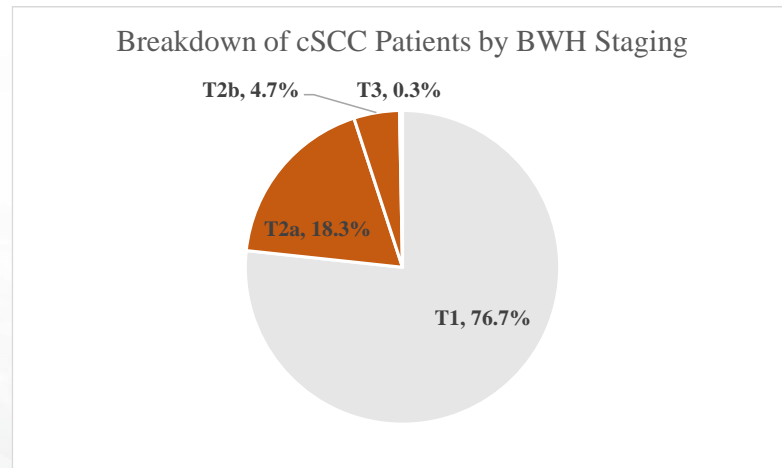
## Staging from Brigham & Women’s Hospital (BWH) Researchers

BWH Tumor Stage	Description
T1	0 high-risk factors*
T2a	1 high-risk factor
T2b	2-3 high-risk factors
T3	≥ 4 high-risk factors



\*Note: High-risk factors include tumor diameter ≥ 2 cm, poorly differentiated histology, perineural invasion ≥ 0.1 mm, or tumor invasion beyond fat (excluding bone invasion which automatically upgrades tumor to BWH stage T3).

**Compare to high-risk factors from NCCN Guidelines on previous page!**



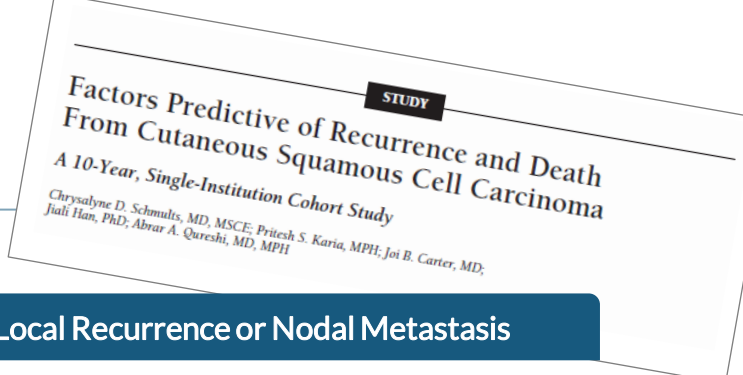
**23.3% of cSCC are stages T2a – T3 (high-risk, i.e., at least 1 risk factor)**

**At 1.8 million cSCC incidences per year, that translates into ~419k high-risk cases per year!**

Source: [Evaluation of American Joint Committee on Cancer, International Union Against Cancer, and Brigham and Women's Hospital Tumor Staging for Cutaneous Squamous Cell Carcinoma](#)  
 Pritesh S. Karia, Anokhi Jambusaria-Pahlajani, David P. Harrington, George F. Murphy, Abrar A. Qureshi, and Chrysalynne D. Schmults. *Journal of Clinical Oncology* 2014 32:4, 327-334

# What Are cSCC Outcomes Like?

## Data from Brigham & Women's Hospital (BWH) Researchers



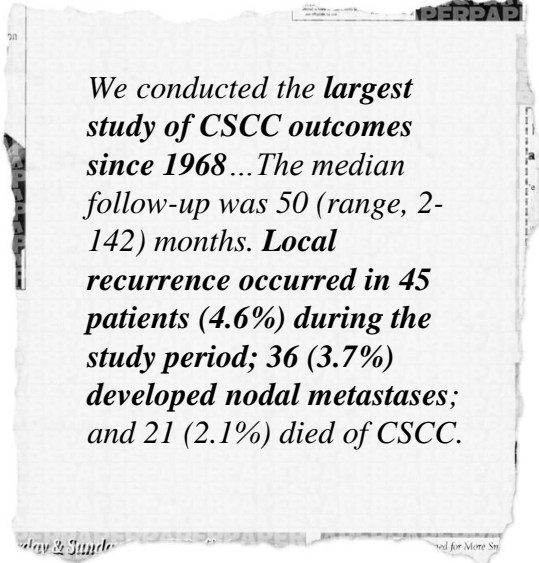
### NCCN Risk Factors Correspond to Recurrence and Metastatic Outcomes

Table 3. Results of Univariate Analysis for Outcomes of Interest

	LR		NM		DSD		ACD	
	SHR (95% CI)	P Value	SHR (95% CI)	P Value	SHR (95% CI)	P Value	HR (95% CI)	P Value
Age, y								
<70	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
70-80	2.1 (1.1-3.9)	.02	1.2 (0.6-2.5)	.66	1.1 (0.4-2.7)	.89	1.7 (1.4-2.0)	<.001
>80	1.7 (0.8-3.8)	.17	1.0 (0.4-2.8)	.99	0.9 (0.2-3.3)	.88	2.5 (2.0-3.1)	<.001
Sex								
Female	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Male	1.6 (0.9-3.0)	.11	2.4 (1.0-5.5)	.04	2.8 (1.9-8.3)	.06	1.9 (1.6-2.3)	<.001
Tumor diameter, cm								
<2	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
≥2	8.9 (5.1-15.7)	<.001	15.2 (6.6-35.2)	<.001	28.5 (9.4-86.3)	<.001	1.0 (0.8-1.3)	.75
Tumor differentiation								
Well	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Moderate	2.7 (1.3-5.9)	.01	5.6 (1.6-19.1)	.006	2.5 (0.6-11.2)	.23	1.3 (1.1-1.6)	.02
Poor	10.4 (5.4-19.0)	<.001	29.8 (10.2-87.0)	<.001	19.4 (6.4-58.5)	<.001	1.7 (1.3-2.1)	<.001
Tumor depth								
Dermis	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Subcutaneous fat	5.9 (3.0-11.7)	<.001	7.2 (2.8-18.1)	<.001	8.8 (2.8-27.8)	<.001	1.5 (1.1-2.0)	.006
Beyond fat	24.4 (12.9-46.1)	<.001	43.0 (19.6-93.2)	<.001	51.4 (19.1-137.8)	<.001	1.7 (1.2-2.6)	.008
Perineural invasion								
No	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Yes	8.8 (4.8-16.4)	<.001	14.5 (7.1-29.8)	<.001	11.3 (4.5-28.1)	<.001	1.7 (1.2-2.3)	.003
Lymphovascular invasion								
No	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Yes	5.7 (2.4-13.4)	<.001	2.7 (0.6-11.3)	.17	2.1 (0.3-15.3)	.47	1.3 (0.8-2.1)	.33
Tumor location								
Other	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Head or neck (excluding ear and temple)	2.5 (1.5-4.4)	.001	2.4 (1.3-5.0)	.009	1.8 (0.8-4.3)	.18	1.1 (0.9-1.3)	.34
Ear	3.8 (1.4-10.4)	.01	3.1 (0.9-11.0)	.03	2.6 (0.8-9.0)	.12	1.4 (1.0-1.9)	.03
Temple	3.2 (1.1-9.0)	.03	3.8 (1.2-12.5)	.03	1.8 (0.2-13.5)	.56	1.5 (1.0-2.3)	.07
Perianal	17.4 (4.1-72.4)	<.001	64.3 (12.4-321.1)	<.001	39.0 (10.7-142.4)	<.001	1.0 (0.3-4.0)	.79
Genitalia	15.0 (2.6-88.2)	.003	69.4 (14.6-329.8)	<.001	47.6 (8.0-282.4)	<.001	0.9 (0.2-5.4)	.78

Abbreviations: ACD, all-cause death; DSD, disease-specific death; HR, hazard ratio; LR, local recurrence; NM, nodal metastasis; SHR, subhazard ratio.

### Estimate of Patient Pool with Local Recurrence or Nodal Metastasis



1.8 million incidences per year, with 4.6% local recurrence and another 3.7% nodal metastasis, translates into ~148 thousand recurrent / metastatic cases per year

Source: [Factors Predictive of Recurrence and Death From Cutaneous Squamous Cell Carcinoma: A 10-Year, Single-Institution Cohort Study](#) Schmults CD, Karia PS, Carter JB, Han J, Qureshi AA. JAMA Dermatol. 2013;149(5):541-547. doi:10.1001/jamadermatol.2013.2139